<u>Claims</u>

1. A method of identifying or predicting the predisposition of coronary artery disease in a subject comprising:

(i) determining the level of gene expression of at least one gene selected from Table 6 in a subject to provide a first value,

(ii) determining the level of gene expression of said at least one gene selected from Table 6 in a control or reference standard to provide a second value and

(iii) comparing whether there is a difference between said first value and second value.

2. A method according to claim 1 wherein said control or reference standard is determined from a subject or group of subjects without coronary artery disease.

3. A method according to claim 1 or 2 wherein the first value is greater than the second value is indicative of the presence or prediction of coronary artery disease.

4. A method according to any one of claims 1-3 wherein the prediction of the presence of coronary artery disease has a probability of at least 50%.

5. A method according to any one of claims 1-4 wherein the first value is at least 20% greater than the second value.

6. A method according to any one of claims 1-5 wherein the level of gene expression of at least one gene selected from the group of genes consisting of:

(i) with the accession codes: BG537190, L37033, AL581768, AF055000, NM025241, AF151074, AF279372 and BF432478 (Table 6) or

(ii) with sequence numbers: SEQ ID No.1, SEQ ID. No.2, SEQ ID No. 3, SEQ ID No. 4, SEQ ID No. 5, SEQ ID No. 6, SEQ ID No. 7 and SEQ ID. No.8 (Table 7) is determined.

7. A method according to any one of claims 1-5 wherein the level of gene expression of at least one gene selected from the group of genes consisting of: PMS2L5 (SEQ ID NO. 9), RXRA (SEQ ID NO. 10), GCN5L1 (SEQ ID NO. 11), CABIN1 (SEQ ID NO. 12), LGALS9 (SEQ ID NO. 13), CEBPA (SEQ ID NO. 14), LRRN4 (SEQ ID NO. 15), STXBP2 (SEQ ID NO. 16), SH3BP2 (SEQ ID NO. 17), RNF24 (SEQ ID NO. 18), PLAUR (SEQ ID NO. 19), RIS1 (SEQ ID NO. 20), ADD1 (SEQ ID NO. 21), GPSM3 (SEQ ID NO. 22), BC002942 (SEQ

50

SUBSTITUTE SHEET (RULE 26)

ID NO. 23), TNFRSF5 (SEQ ID NO. 24), N4BP1 (SEQ ID NO. 25), FLJ12438 (SEQ ID NO. 26) and MMP24 (SEQ ID NO. 27) of Table 9 is determined.

8. A method according to any one of claims 1-5 wherein the level of gene expression of at least one gene selected from the group of genes consisting of: PTP4A1 (SEQ ID NO. 28), PAFAH1B1 (SEQ ID NO. 29), SOX4 (SEQ ID NO. 30), ASNA1 (SEQ ID NO. 31), MAN2A2 (SEQ ID NO. 32), NFYC (SEQ ID NO. 33), NOTCH2 (SEQ ID NO. 34), HDAC5 (SEQ ID NO. 35), HCFC1 (SEQ ID NO. 36), NFX1 (SEQ ID NO. 37), CRSP2 (SEQ ID NO. 38), ICAM1 (SEQ ID NO. 39), PSG3 (SEQ ID NO. 40), STC2 (SEQ ID NO. 41) and SEMA3C (SEQ ID NO. 42) of Table 10 is determined.

9. A method according to any one of claims 1-8 wherein the levels of gene expression of at least one gene selected from the genes of Table 7 and/or of at least one gene selected from Table 9 and/or Table 10 are determined.

10. A method of identifying or predicting coronary artery disease (CAD) in a subject comprising:
(a)   determining the level of one or more peptides selected from Table 11 in a subject to provide a first value,
(b)   determining the level of said one or more peptides selected from Table 11 in a control or reference standard to provide a second value and
(c)   comparing whether there is a difference between said first value and second value.

11. A method according to claim 10 wherein the compared peptide level is increased in an identification or prediction of coronary artery disease for those peptides of Table 11 wherein Disease > Control or for those peptides of Table 11 wherein the peptide is Predominant in Disease.

12. A method according to claim 11 wherein the compared peptide level is decreased in an identification or prediction of coronary artery disease for those peptides of Table 11 wherein Control > Disease or for those peptides of Table 11 wherein the peptide is Predominant in Control.

51

13. A method according to any one of claims 1 to 12 comprising

(a) determining the level of one or more peptides selected from Table 11 and the level of gene expression of at least one gene selected from Table 6 and/or Table 7 and/or Table 9 and/or Table 10 in a subject to provide a first value,

(b) determining the level of said one or more peptide selected from Table 11 and the level of gene expression of said at least one gene selected from Table 6 and/or Table 7 and/or Table 9 and/or Table 10 in a control or reference standard to provide a second value, and

(c) comparing whether there is a difference between said first value and second value, wherein an elevated peptide level in the first value for the one or more Disease > Control and/or Predominant in Disease peptide of Table 11 and/or wherein a decrease of peptide level in the first value for the one or more Control > Disease and/or Predominant in Control peptide of Table 11 and wherein an elevated level of gene expression of the at least one gene selected from Table 6 and/or Table 7 and/or Table 9 and/or Table 10 in the first value is an identification or prediction of coronary artery disease.

14. A method according to any one of claims 1-6, 9 or 13 wherein the level of gene expression of the at least one gene corresponding to SEQ ID NO. 1 from Table 7 is determined.

15. A method according to any one of claims 1-6, 9, 13 or 14 wherein the levels of gene expression of at least two to eight sequences selected from Table 7 are determined.

16. A method according to any one of claims 1-6, 9, or 13-15 wherein the levels of gene expression of a plurality of genes selected from Table 7 are determined.

17. A method according to any one of claims 1-6, 9, or 13-16 wherein the level of gene expression of all eight genes selected from Table 7 is determined.

18. A method according to any one of claims 1-5, 7, 9 or 13 wherein the level of gene expression of the at least one gene corresponding to SEQ ID NO. 9 from Table 9 is determined.

19. A method according to any one of claims 1-5, 7, 9, 13 or 18 wherein the levels of gene expression of at least two to nineteen genes selected from Table 9 are determined.

SUBSTITUTE SHEET (RULE 26)

20. A method according to any one of claims 1-5, 7, 9, 13, 18 or 19 wherein the levels of gene expression of a plurality of genes selected from Table 9 are determined.

21. A method according to any one of claims 1-5, 7, 9, 13, 18-20 wherein the levels of gene expression of all nineteen genes selected from Table 9 are determined.

22. A method according to any one of claims 1-5, 8, 9 or 13 wherein the level of gene expression of the at least one gene corresponding to SEQ ID NO. 28 from Table 10 is determined.

23. A method according to any one of claims 1-5, 8, 9, 13 or 22 wherein the levels of gene expression of at least two to fifteen genes selected from Table 10 are determined.

24. A method according to any one of claims 1-5, 8, 9, 13, 22 or 23 wherein the levels of gene expression of a plurality of genes selected from Table 10 are determined.

25. A method according to any one of claims 1-5, 8, 9, 13, 22-24 wherein the levels of gene expression of all fifteen genes selected from Table 10 are determined.

26. A method according to any one of claims 10-13 wherein the peptide level of a plurality of peptide selected from Table 11 is determined.

27. A method according to any one of claims 10-13 or 26 wherein the peptide level of all peptides selected from Table 11 are determined.

28. A method according to any one of claims 10-13, 26 or 27 wherein said peptide level is measured in a blood, plasma or serum sample.

29. A method according to any one of claims 1-9, or 13-28 wherein determination of the level of gene expression comprises measuring the protein expression product.

53

SUBSTITUTE SHEET (RULE 26)

30. A method according to any one of claims 10-13 or 29 wherein the amount of said protein expression product and/or the amount of peptide is detected using an antibody, antibody derivative or antibody fragment, which specifically binds to the protein.

31. A method according to any one of claims 1-9, or 13-28 wherein determination of the level of gene expression comprises measuring the gene expression of a transcribed polynucleotide of the gene.

32. A method according to claim 31 wherein the transcribed polynucleotide is mRNA or cDNA.

33. A method according to claim 31 or 32 wherein the level of expression is detected by microarray analysis, Northern blot analysis, reverse transcription PCR or RT-PCR .

34. A method according to any one of claims 1-33 wherein said level of gene expression and/or the level of peptide is measured ex vivo in a sample selected from the group of: blood, serum, plasma, lymph, urine, tear, saliva, cerebrospinal fluid, leukocyte sample or tissue sample.

35. A method according to any one of claims 1-34 wherein said method further comprises the measurement of CAD-Index.

36. A method according to claim 35 wherein a CAD Index between 23-100 is indicative of the probability of the presence or predisposition of coronary artery disease.

37. A method of monitoring a subject identified as having coronary artery disease before and after treatment comprising:
(i) determining the level of gene expression of at least one gene from Table 6 or Table 7 in said subject prior to treatment providing a first value,
(ii) determining the level of gene expression of the same at least one gene as in (i) after treatment providing a second value and
(iii) comparing the difference in the level of gene expression of said subject before treatment and after treatment.

SUBSTITUTE SHEET (RULE 26)

38. A method of monitoring a subject identified as having coronary artery disease before and after treatment comprising:

(i) determining the level of gene expression of at least one gene from Table 9 or Table 10 in said subject prior to treatment providing a first value,

(ii) determining the level of gene expression of the same at least one gene as in (i) after treatment providing a second value and

(iii) comparing the first and the second value.

39. A method of monitoring a subject identified as having coronary artery disease before and after treatment comprising:

(i) determining the level of gene expression of at least one gene selected of Table 7 and/or of at least one gene of Table 9 and/or Table 10 in said subject prior to treatment providing a first value,

(ii) determining the level of gene expression of the same genes as in (i) after treatment providing a second value and

(iii) determing the difference in the level of gene expression of said subject before treatment and after treatment by comparing the first with the second value.

40. A method of monitoring a subject identified as having coronary artery disease before and after treatment comprising:

(i) determining the level of one or more peptide selected from Table 11 and the level of gene expression of at least one gene from Table 6 and/or Table 7 and/or Table 9 and/or Table 10 in said subject prior to treatment providing a first value,

(ii) determining the level of the one or more peptide and the level of gene expression of the same at least one gene as in (i) after treatment providing a second value and

(iii) determing the difference in the level of the one or more peptide and in the level of gene expression of said subject before treatment and after treatment by comparing the first with the second value.

41. A method of monitoring a subject according to any one of claims 37-40 further comprising:

(iv) determining that a difference in the level of gene expression and/or level of peptide corresponds to the efficacy of the treatment of coronary artery disease in said subject.

SUBSTITUTE SHEET (RULE 26)

42. A method of monitoring a subject according to any one of claims 37-41 wherein a positive response to the treatment is measured when the second value for the level of gene expression is less than the first value.

43. A method of monitoring a subject according to claim 40 or 41 wherein a decrease in peptide level in the second value for the one or more Disease > Control and/or Predominant in Disease peptide of Table 11; and/or wherein an increase in peptide level in the second value for the one or more Control > Disease and/or Predominant in Control peptide of Table 11, and/or wherein a decrease of level of gene expression of the at least one gene selected from Table 6 and/or Table 7 and/or Table 9 and/or Table 10 in the second value indicates a positive response to the treatment.

44. A method of monitoring a subject according to any one of claims 37, 39-43 wherein the level of gene expression of at least SEQ ID No. 1 is determined.

45. A method of monitoring a subject according to any one of claims 37, 39-44 wherein the level of gene expression of a plurality of genes in Table 7 is determined.

46. A method of monitoring a subject according to any one of claims 37, 39-45 wherein the level of gene expression of all 8 genes listed in Table 7 is determined.

47. A method of monitoring a subject according to any one of claims 38-43 wherein the level of gene expression of the at least SEQ ID NO. 9 from Table 9 is determined.

48. A method of monitoring a subject according to any one of claims 38-43, or 47 wherein the levels of gene expression of at least two to nineteen genes selected from Table 9 are determined.

49. A method of monitoring a subject according to any one of claims 38-43, 47 or 48 wherein the levels of gene expression of a plurality of genes selected from Table 9 are determined.

50. A method of monitoring a subject according to any one of claims 38-43, or 47-49 wherein the levels of gene expression of all nineteen genes selected from Table 9 are determined.

SUBSTITUTE SHEET (RULE 26)

51. A method of monitoring a subject according to any one of claims 38-43 wherein the level of gene expression of at least SEQ ID NO. 28 from Table 10 is determined.

52. A method of monitoring a subject according to any one of claims 38-43, or 51 wherein the levels of gene expression of at least two to fifteen genes selected from Table 10 are determined.

53. A method of monitoring a subject according to any one of claims 38-43, 51 or 52 wherein the levels of gene expression of a plurality of genes selected from Table 10 are determined.

54. A method of monitoring a subject according to any one of claims 38-43, or 51-53 wherein the levels of gene expression of all fifteen genes selected from Table 10 are determined.

55. A method of monitoring a subject according to any one of claims 40-43 wherein the level of a plurality of peptides of Table 11 and the level of gene expression of a plurality of genes selected from the genes of Table 6 and/or Table 7 and/or Table 9 and/or Table 10 are determined.

56. A method of monitoring the progression or severity of coronary artery disease comprising
(i) determining the level of gene expression of at least one gene from Table 6 or Table 7 at an initial time point providing a first value,
(ii) determining the level of gene expression of at least one gene from Table 6 or Table 7 at a time point after the initial time point providing a second value;
(iii) comparing the difference in the level of gene expression of the first value to the second value wherein a higher level of gene expression in the second value is indicative of an increase in severity of coronary artery disease.

57. A method of monitoring the progression or severity of coronary artery disease comprising
(i) determining the level of gene expression of at least one gene from Table 7 and/or Table 9 and/or Table 10,
(ii) determining the level of gene expression of the same at least one gene as in (i) at a time point after the initial time point providing a second value,

SUBSTITUTE SHEET (RULE 26)

(iii) comparing the difference in the level of gene expression of the first value to the second value wherein a higher level of gene expression in the second value is indicative of an increase in severity of coronary artery disease.

58. A method according to claim 56 or 57 wherein a lower level of gene expression in the second value is indicative of a decrease in severity of coronary artery disease.

59. A method of monitoring the progression or severity of coronary artery disease comprising

(i) determining the level of one or more peptide selected from Table 11 and the level of gene expression of at least one gene from Table 6 and/or Table 7 and/or Table 9 and/or Table 10 at an initial time point providing a first value,

(ii) determining the level of the one or more peptide and the level of gene expression of the same at least one gene as in (i) at a time point after the initial time point providing a second value,

(iii) comparing the difference in the level of the one or more peptides and gene expression of the first value to the second value wherein a higher level of the one or more Disease > Control and/or Predominant in Disease peptide or a lower level of the Control > Disease peptides or the Predominant in Control peptides of Table 11 in the second value, and a higher level of expression of the at least one gene from Table 6 and/or Table 7 and/or Table 9 and/or Table 10 in the second value is indicative of an increase in severity of coronary artery disease.

60. A method of screening candidate agents for use in treatment of coronary artery disease comprising:

(i) contacting a cell or sample of cells capable of expressing a gene selected from Table 6 or Table 7 with a candidate agent ex vivo,

(ii) determining the level of gene expression of said at least one gene from Table 6 or Table 7 to provide a first value,

(iii) determining the level of gene expression of the same at least one gene from Table 6 or Table 7 in a cell or sample of cells in the absence of the candidate agent to provide a second value, and

(iv) comparing the first value with the second value wherein a difference in level of gene expression is indicative of an agent potentially capable of being used for the treatment of coronary artery disease.

SUBSTITUTE SHEET (RULE 26)

61. A method of screening candidate agents for use in treatment of coronary artery disease comprising:

(i) contacting a cell or sample of cells capable of expressing at least one gene selected from Table 7 and/or Table 9 and/or Table 10 with a candidate agent ex vivo,

(ii) determining the level of gene expression of the at least one gene of (i) to provide a first value,

(iii) determining the level of gene expression of the at least one gene gene of (i) and (ii) in a cell or sample of cells in the absence of the candidate agent to provide a second value, and

(iv) comparing the first value with the second value, wherein a difference in level of gene expression is indicative of an agent potentially capable of being used for the treatment of coronary artery disease.

62. A method of screening according to claim 61 or 62 wherein a decrease in the level of gene expression in the presence of a candidate agent is determined when the first value is lower than the second value and is indicative of an agent potentially capable of being used for the treatment of coronary artery disease.

63. A method of screening candidate agents for use in treatment of coronary artery disease comprising:

(i) contacting a cell or sample of cells capable of producing at least one peptide selected from Table 11 and capable of expressing at least one gene selected from Table 6 and/or Table 7 and/or Table 9 and/or Table 10 with a candidate agent ex vivo,

(ii) determining the level of the one or more peptide of (i) and the level of gene expression of the at least one gene of (i) to provide a first value,

(iii) determining the level of the one or more peptide of (i) and the level of gene expression of the at least one gene of (i) in a cell or sample of cells in the absence of the candidate agent to provide a second value, and

(iv) comparing the first value with the second value wherein a difference in the level of the one or more peptide and in the level of gene expression of the at least one gene is indicative of an agent potentially capable of being used for the treatment of coronary artery disease.

64. A method of screening according to claims 63 wherein a lower level in the first value of the at least one Disease > Control peptide and/or Predominant in Disease peptide and/or an

higher level in the first value of the at least one Control > Disease and/or Predominant in Control peptide from Table 11 and wherein a lower level in the first value of the at least one gene selected from Table 6 and/or Table 7 and/or Table 9 and/or Table 10 when compared to the second value is indicative of an agent potentially capable of being used for the treatment of coronary artery disease.

65. A method of screening according to any one of claims 60-64 wherein the level of gene expression of at least SEQ ID No. 1 is determined.

66. A method of screening according to any one of claims 60-65 wherein the level of gene expression of a plurality of genes selected from Table 7 is determined.

67. A method of screening according to any one of claims 60-66 wherein the level of gene expression of all eight genes selected from Table 7 is determined.

68. A method of screening according to any one of claims 61-64 wherein the level of gene expression of at least SEQ ID No. 9 of Table 9 is determined.

69. A method of screening according to any one of claims 61-64, or 68 wherein the levels of gene expression of a plurality of genes selected from Table 9 are determined.

70. A method of screening according to any one of claims 61-64, 68 or 69 wherein the levels of gene expression of all nineteen genes selected from Table 9 are determined.

71. A method of screening according to any one of claims 61-64 wherein the level of gene expression of at least SEQ ID No. 28 of Table 10 is determined.

72. A method of screening according to any one of claims 61-64, or 71 wherein the levels of gene expression of a plurality of genes selected from Table 10 are determined.

73. A method of screening according to any one of claims 61-64, 71 or 72 wherein the levels of gene expression of all nineteen genes selected from Table 10 are determined.

SUBSTITUTE SHEET (RULE 26)

74. A method of screening according to claims 63 or 64 wherein the level of a plurality of peptides of Table 11 and the levels of gene expression of a plurality of genes selected from Table 6, 7, 9 and/or Table 10 are determined.

75. A method of treating or preventing coronary artery disease comprising administering to a subject an effective amount of an agent that can induce a decrease in the level of gene expression, synthesis, or activity of at least one gene or gene expression product from Table 6 or Table 7.

76. A method of treating or preventing coronary artery disease comprising administering to a subject an effective amount of an agent that can induce a decrease in the level of gene expression, synthesis, or activity of at least one gene or gene expression product from Table 7 and/or Table 9 and/or Table 10.

77. A method of treating or preventing coronary artery disease comprising administering to a subject an effective amount of an agent that can induce a decrease in the level of at least one Disease > Control and/or Predominant in Disease peptide and/or an increase in the level of at least one Control > Disease and/or Predominant in Control peptide from Table 11 and/or a decrease in gene expression, synthesis, or activity of at least one gene or gene expression product from Table 6 and/or Table 7 and/or Table 9 and/or Table 10.

78. A method according to any one of claims 75-77 wherein said agent is selected from the group consisting of antisense oligonucleotides, double stranded RNA, ribozyme, small molecule, antibody or antibody fragment.

79. A method of manufacture of a medicament for the treatment or prevention of coronary artery disease comprising an effective amount of an agent that can induce a decrease in the level of gene expression, synthesis, or activity of at least one gene or gene expression products from Table 6 or Table 7 and/or Table 9 and/or Table 10.

80. The use of a substance comprising an effective amount of an agent that can induce a decrease in the level of gene expression, synthesis, or activity of at least one gene or gene expression product from Table 6 or Table 7 and/or Table 9 and/or Table 10 in the manufacture of a medicament for the treatment or prevention of coronary artery disease.

SUBSTITUTE SHEET (RULE 26)

81. The use of a substance comprising an effective amount of an agent that can induce a decrease in the level of at least one Disease > Control and/or Predominant in Disease peptide and/or induce an increase in the level of at least one Control > Disease and/or Predominant in Control peptide from Table 11 and/or a decrease in gene expression, synthesis, or activity of at least one gene or gene expression product from Table 6 or Table 7 and/or Table 9 and/or Table 10 in the manufacture of a medicament for the treatment or prevention of coronary artery disease.

82. A kit for the identifying or predicting the predisposition coronary artery disease in a subject comprising:
(i) instructions for determining the level of gene expression of at least one gene from Table 6 or Table 7 and
(ii) control or reference standard level of gene expression from a normal subject or subjects without coronary artery disease for at least one gene in Table 6 or Table 7.

83. A kit for the identifying or predicting the predisposition coronary artery disease in a subject comprising:
(i) instructions for determining the level of gene expression of at least one gene selected from Table 7 and/or Table 9 and/or Table 10,
(ii) control or reference standard level of gene expression from a normal subject or subjects without coronary artery disease for the genes of (i).

84. A kit according to claim any one of claims 82-83 wherein additionally antibodies, antibody derivatives or antibody fragments capable of binding to a polypeptide encoded by the at least one gene from Table 6, and/or Table 7, and/or Table 9 and/or Table 10 are provided.

85. A kit for the identifying or predicting coronary artery disease in a subject comprising:
(a) instructions for determining the peptide level of at least one peptide from Table 11 and
(b) control or reference standard peptide level from a normal subject or subjects without coronary artery disease for at least one peptide in Table 11.

86. A kit according to claim 85, further comprising
(c) an antibody that binds to said at least one peptide from Table 11.

SUBSTITUTE SHEET (RULE 26)

87. A kit for the identifying or predicting coronary artery disease in a subject comprising:

(a) instructions for determining the peptide level of at least one peptide from Table 11 and for determining the level of gene expression of at least one gene selected from Table 6 and/or Table 7 and/or Table 9 and/or Table 10 and

(b) control or reference standard peptide level from a normal subject or subjects without coronary artery disease for the at least one peptide in Table 11 and for determining the level of gene expression of at least one gene of Table 6 and/or Table 7 and/or Table 9 and/or Table 10 of (i)

88. A kit according to claim 87, further comprising

(c) an antibody that binds to said at least one peptide from Table 11 and additionally antibodies, antibody derivatives or antibody fragments capable of binding to a polypeptide encoded by the at least one gene from Table 6, and/or Table 7, and/or Table 9 and/or Table 10 are provided.

SUBSTITUTE SHEET (RULE 26)